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CLAIMPTO

WNP

12/21/2004

1. **(Currently Amended)** A method of eliciting broad spectrum protective immunity against *Neisseria meningitidis*, said method comprising the steps of:

administering to a mammal a first preparation of microvesicles (MVs) from a first *Neisseria meningitidis* species that is a member of a first serotype and of a first serosubtype, in an amount sufficient to elicit an immune response to epitopes present in said first preparation; and

administering to said mammal a second preparation of MVs from a second *Neisseria meningitidis* species that is a member of a second serotype and of a second serosubtype, in an amount sufficient to elicit an immune response to epitopes present in said second preparation;

wherein the serotype or serosubtype of each of the first and second ~~first, second, and third~~ *Neisseria meningitidis* species is different, and wherein administering of the first and second ~~first, second, and third~~ preparations is sufficient to elicit an immune response in said mammal, wherein said immune response confers protective immunity against ~~a disease caused by more than one strain of~~ *Neisseria meningitidis* species.

2. (Original) The method of claim 1, the method further comprising:

administering to said mammal a third preparation of outer membrane vesicles (OMV), MVs, or both OMVs and MVs from a third *Neisseria meningitidis* species that is a member of a third serotype and of a third serosubtype, in an amount sufficient to elicit an immune response to epitopes present in said third preparation.

3. (Original) The method of claim 2, wherein the first, second, and third preparations are administered serially.

4. (Original) The method of claim 3, wherein the preparations are administered such that the first preparation is administered first, the second preparation administered second, and third preparation administered third.

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5. (Currently Amended) The method of claim 1, wherein the ~~first, second, and third~~ first and second preparations are administered as a mixture.

6. (Original) The method of claim 1, wherein the third preparation comprises MVs.

7. (Currently Amended) The method of claim 1, wherein ~~the~~ protective immunity is conferred ~~is~~ against ~~a disease~~ at least four strains of *Neisseria meningitidis* species.

8. (Currently Amended) The method of claim 7, wherein protective immunity conferred is against ~~a disease caused by~~ more than one strain of serogroup B *Neisseria meningitidis* species.

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20. (Previously Presented) The method of claim 1, wherein the OMV and MV preparations are administered together with pharmaceutically acceptable excipients.

21. (Currently Amended) The method of ~~claim 1~~ claim 20, wherein the excipients comprise an adjuvant.

22. (Currently Amended) The method of ~~claim 1~~ claim 21, wherein the adjuvant is selected from the group consisting of aluminum phosphate, aluminum hydroxide, alum or MF59.

23. (Previously Presented) The method of claim 1, wherein administering is by injection.

24. (Previously Presented) The method of claim 1, wherein administering is oral or by aerosol administration.

25. (Previously Presented) The method of claim 1, wherein the mammal is a human.

26. (Original) The method of claim 25, wherein the human is immunologically naïve with respect to *Neisseria meningitidis*.

27. (Original) The method of claim 25, wherein the human is a human child less than five years old.

41. (New) The method of claim 1, wherein the first and second preparations are treated to reduce endotoxin.

42. (New) The method of claim 41, wherein endotoxin reduction is by detergent extraction with a detergent other than deoxycholate.

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9. (Currently Amended) A method of eliciting broad spectrum protective immunity against a ~~disease caused by a member of serogroup B of~~ *Neisseria meningitidis*, said method comprising the steps of:

administering to a mammal a first preparation of microvesicles (MVs) from a first *Neisseria meningitidis* species that is a member of a first serosubtype, in a amount sufficient to elicit an immune response to epitopes present in said first preparation;

administering to said mammal a second preparation of MVs from a second *Neisseria meningitidis* species that is a member of a second serosubtype, in a amount sufficient to elicit an immune response to epitopes present in said second preparation;

wherein the serosubtype of each of the first and second *Neisseria meningitidis* species is different, and wherein administering of the first and second preparations is sufficient to elicit an immune response in said mammal, wherein said immune response confers protective immunity against a disease ~~caused by~~ at least four strains of *Neisseria meningitidis* species.

10. (Original) The method of claim 9, wherein the method further comprises administering to said mammal a third preparation from a third *Neisseria meningitidis* species that is a member of a third serosubtype, the third preparation comprising outer membrane vesicles (OMV), MVs, or both OMVs and MVs, said administering being in an amount sufficient to elicit an immune response to epitopes present in said third preparation, wherein the serosubtype of the first and third species is different.

12. (Original) The method of claim 9, wherein the first and second preparations are administered as a mixture.

13. (Original) The method of claim 9, wherein the first and second preparations are administered serially.

43. (New) The method of claim 9, wherein the first and second preparations are treated to reduce endotoxin.

44. (New) The method of claim 43, wherein endotoxin reduction is by detergent extraction with a detergent other than deoxycholate.

14. **(Currently Amended)** A method of eliciting broad spectrum protective immunity against a disease caused by a *Neisseria meningitidis* species, said method comprising the steps of:

administering to a mammal a first preparation from a first *Neisseria meningitidis* species, the first preparation comprising outer membrane vesicles (OMV), microvesicles (MV), or both OMV and MV, said administering of the first preparation being in an amount sufficient to elicit an immune response to epitopes present in said first preparation;

administering to the mammal a second preparation from a second *Neisseria meningitidis* species that is genetically diverse to the first *Neisseria meningitidis* species, the second preparation comprising outer membrane vesicles (OMV), microvesicles (MV), or both OMV and MV, said administering of the second preparation being in an amount sufficient to elicit an immune response to epitopes present in said second preparation;

wherein administering of the first and second preparations elicits an immune response in said mammal, wherein said immune response confers protective immunity against a disease caused more than one strain of *Neisseria meningitidis* species.

15. **(Original)** The method of claim 14, comprising the additional step of administering to said mammal a third preparation of outer membrane vesicles from a third *Neisseria meningitidis* species, which third species that is genetically diverse to at least the first *Neisseria meningitidis* species, said administering being in an amount sufficient amount to elicit an immune response to epitopes present in said third preparation.

40. **(New)** The method of claim 14, wherein the first and second preparations are administered serially.

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45. (New) The method of claim 14, wherein the first and second preparations are treated to reduce endotoxin.

46. (New) The method of claim 45, wherein endotoxin reduction is by detergent extraction with a detergent other than deoxycholate.

47. (New) A method of eliciting broad spectrum protective immunity against a disease caused by a *Neisseria meningitidis* species, said method comprising the steps of:

administering to a mammal a first preparation from a first *Neisseria meningitidis* species that is a member of a first serotype and of a first serosubtype, the first preparation comprising outer membrane vesicles (OMV), microvesicles (MV), or both OMV and MV, said administering of the first preparation being in an amount sufficient to elicit an immune response to epitopes present in said first preparation;

administering to the mammal a second preparation from a second *Neisseria meningitidis* species that is a member of a second serotype and of a second serosubtype, the second preparation comprising outer membrane vesicles (OMV), microvesicles (MV), or both OMV and MV, said administering of the second preparation being in an amount sufficient to elicit an immune response to epitopes present in said second preparation;

wherein the serotype or serosubtype of each of the first and second *Neisseria meningitidis* species is different, and wherein administering of the first and second preparations elicits an immune response in said mammal, wherein said immune response confers protective immunity against more than one strain of *Neisseria meningitidis* species.

48. (New) The method of claim 47, further comprising:

administering to said mammal a third preparation of outer membrane vesicles (OMV), MVs, or both OMVs and MVs from a third *Neisseria meningitidis* species that is a member of a third serotype and of a third serosubtype, in an amount sufficient to elicit an immune response to epitopes present in said third preparation.

49. (New) The method of claim 48, wherein the first, second, and third preparations are administered serially.

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